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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,436	03/19/2004	Mark B. Lyles	068351.0144	7276
31625	7590	12/06/2007		
BAKER BOTTS L.L.P. PATENT DEPARTMENT 98 SAN JACINTO BLVD., SUITE 1500 AUSTIN, TX 78701-4039			EXAMINER SINGH, SATYENDRA K	
			ART UNIT 1657	PAPER NUMBER
			MAIL DATE 12/06/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/804,436

Applicant(s)

LYLES, MARK B.

Examiner

Satyendra K. Singh

Art Unit

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-17, 19 and 20 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-17, 19 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response and amendments to the claims filed with the office on September 27th 2007 is duly acknowledged.

Claims 1-10 (non-elected invention of group I) are withdrawn from further consideration.

Claim 18 is canceled by applicant's current amendment to claims.

Claims 11-17, 19 and 20 (group II, as currently amended) are examined on their merits in this office action.

The following contains new grounds of rejection necessitated by applicant's current amendment to the pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 11-17, 19 and 20 (as currently amended) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites "**suspending a subject's autologous stem cells in a soluble medium**", which is confusing. It is unclear as to what exactly is encompassed by the method step as recited in the claim. It is unclear as how, from which tissue and how much of said "autologous stem cells" are obtained from the subject in order to be suspended in a soluble medium, as required by the limitation as claimed. In addition, said recitation is also ambiguous as it reads on a method that uses a composition (i.e. cell suspension)

that only has "a subject's autologous stem cells" and is not open to further additions (see instant claims 16 and 17, in particular). Appropriate explanation/correction is required.

Since, claims 12-17, 19 and 20 depend from the broader claim 11, they are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claims 16 and 17 recite the limitation "**autologous cells**" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 11 is directed specifically to "stem cells".

3. Claim 19 recites the limitation "**at least two types of autologous cells**" in line 2. There is insufficient antecedent basis for this limitation in the claim, since claim 11 can be interpreted as a closed claim, i.e. not open to the addition of further ingredients.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claim 11, 14-17 and 20 (as currently amended) are/remain rejected under 35 U.S.C. 102(b) as being anticipated by COHEN et al (2000; [U]).

Claims 11-17, 19 and 20 (as currently amended) are generally directed to a **method of dispersing living cells** comprising: suspending a subject's autologous stem cells in a soluble medium; placing the cells into a receptacle of an air-jet sprayer (having a nozzle orifice with a pore size sufficient to

allow passage of cells without damage); and dispersing the cells onto an area of skin of the subject lacking normal, healthy skin using the air-jet sprayer (see detailed recitations of instant claims 14-17 and 20).

Cohen et al [U] teach a method of dispersing living skin epidermal cells isolated from the skin of groin area (see abstract, and page 1210, *Materials and Methods*, in particular) comprising suspending **autologous cells** in a soluble medium (such as RPMI 1640 transport medium containing epidermal cells that are made of keratinocytes, fibroblasts, and **stem cells**; growth factor such as fetal calf serum; antibiotics such as penicillin and streptomycin; and an adhesion factor such as fibrin glue, Tisseel VH; see pages 1210-1211, right column, in particular); placing the cells into a receptacle (see figure 1 for the device and parts, page 1208, in particular) of an air-jet sprayer (a commercial, **three-component aerosolization device** that uses compressed air, as shown in figure 1; having a nozzle orifice with a pore size sufficient to allow passage of cells without damage); and dispersing the cells onto an area of skin of a subject lacking normal, healthy skin (using pigs as experimental animals with full-thickness wounds on the back taken as area of skin lacking normal, healthy skin; see pages 1210-1211, in particular) using the air-jet sprayer; wherein the method further comprises growing a three-dimensional epithelial tissue from the cells in the area lacking normal, healthy skin (see table II-III, figures 3 and 5, and page 1212, in particular). In addition, it is to be noted that Cohen et al explicitly suggest an alternative method such as "to use the cells (i.e. **autologous epidermal cells**) along with a dermal graft or dermal substitute" (see Cohen et al, page 1214, left column, 1st paragraph, in particular), and thus **invite such modification and/or combination** in the method of dispersing living cells onto an area

of skin (even with unfavorable topography) of a subject lacking normal, healthy skin using an air-jet spray device, as recited by the instant invention.

Response to Applicant's Arguments

Applicant's arguments filed on September 27th 2007 (as they pertain to the above prior art rejection of record) have been fully considered but they are not persuasive for the following reasons of record.

Applicant argues that Cohen et al "fail to teach or suggest" the utilization of "autologous stem cells" (see response, page 6, 2nd paragraph, in particular), which is not found to be persuasive because the **epidermal cell suspension** prepared and used for aerosolization by Cohen et al contains stem cells in said "epidermal cells" preparation obtained after trypsin/EDTA treatment from the epidermis of the experimental animals (see rejection above, and Cohen et al, page 1210, right column, 2nd paragraph, in particular). Contrary to the argument put forth by the applicant, the epidermal layer of skin is known in the art (see evidentiary support; Watt, [U2], see page 831, summary, and introduction, in particular) to contain stem cells, that were not selectively taken out from the "cell suspension" prepared and used by Cohen et al, and therefore, the cell suspension used by the referenced invention had stem cells, and was applied/aerosolized along with "keratinocytes at different stages of proliferation", a few and fibroblasts and dendritic cells, as disclosed in the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-17, 19 and 20 (as currently amended) are/remain rejected under 35

U.S.C. 103(a) as being unpatentable over MARSHALL et al (US 6,479,052 B1; [A]).

Claims 11-17, 19 and 20 are generally directed to a **method of dispersing living cells** comprising: suspending a subject's autologous stem cells in a soluble medium; placing the cells into a receptacle of an air-jet sprayer (having a nozzle orifice with a pore size sufficient to allow passage of cells without damage); and dispersing the cells onto an area of skin of the subject lacking normal, healthy skin using the air-jet sprayer (see detailed recitations of instant claims 14-17 and 20).

Marshall et al [A] disclose a method of dispersing autologous living cells on a skin wound (for example, keratinocytes, fibroblasts, etc.; see abstract, summary of the invention, column 2, 2nd paragraph; column 4, last paragraph, and claims, in particular) comprising suspending autologous cells in a soluble medium (see example 3, columns 12-13, in particular); placing the cells into a receptacle of **an air-jet sprayer** (having a nozzle orifice with a pore size sufficient to allow passage of cells without damage; see column 7-8); and dispersing the cells onto an area of skin of a subject (experimental animal such as Large White pig; see column 3, 1st paragraph, and example 3, in particular) lacking normal, healthy skin using the air-jet sprayer; wherein the

keratinocytes (i.e. contained in a **cell suspension** having growth factors such as serum) are sprayed (with or without fibrin sealant, i.e. an adhesion factor) onto a **dermal graft** (such as Integra; example 3, column 13, in particular) or onto a tissue scaffold (such as fibrin matrix, or other types of biodegradable polymers; see columns 6-7, in particular).

Furthermore, it is to be noted that Marshall et al [A] clearly suggest and disclose a method of dispersing living cells, wherein various types of autologous cells (including keratinocytes, fibroblasts, etc.) can be delivered separately onto a target (see column 3, 1st paragraph, and column 8, 1st and 2nd paragraphs, in particular), or in combination (i.e. co-dispersed or co-delivered) with other autologous cells, growth factors, bioactive agents, etc. (see column 6, lines 41-46, in particular).

However, a method according to claim 11, wherein the autologous cells comprise **stem cells**, and wherein the method further comprises **separately dispersing** at least two types of autologous cells (see instant claim 19) onto the area of skin of a subject lacking normal, healthy skin using the air-jet sprayer, though suggested, is not explicitly exemplified by the referenced invention of Marshall et al.

Given the fact that Marshall et al explicitly disclose a method for spray delivery of living cells, including keratinocytes (which are known in the art to contain at least some stem cells) with or without fibrin sealant onto a target area such as skin wound, and further disclose spray delivery for the fibroblasts (see column 2, 2nd paragraph, and column 3, 1st paragraph, in particular) and other suitable cells, it would have been obvious to a person of ordinary skill in the tissue-repair or regeneration art (at the time

the claimed invention was made) to modify the method of Marshall et al such that it further includes fibroblasts, or subject's autologous stem cells (for their potential for enhancing tissue repair and regeneration which is well documented in the wound healing prior art) with a reasonable expectation of success.

The specific limitation of separately delivering at least two different types of autologous cells would have been a matter of routine optimization of the method to an artisan of ordinary skill in the art, as evidenced by the fact that Marshall et al disclose individual delivery of autologous keratinocytes, and co-delivery of keratinocytes and fibroblasts (see column 5, 3rd paragraph, column 6, lines 41-46, in particular), and further suggest the fact that the device can be modified to provide more outlets, etc. (see column 8, 1st paragraph, in particular) depending on the need. Therefore, the invention as claimed is fully encompassed by the disclosure of the method of spray delivery of living cells, as disclosed by the prior art, Marshall et al [A].

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the claimed invention was made.

As per MPEP 2144.04, Ex parte Rubin, 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004) (The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Response to Applicant's Arguments

Applicant's arguments filed with the office on September 27th 2007 (as they pertain to the obviousness rejection of record) have been fully considered but they are not persuasive for the following reasons of record.

Applicant's argument (see response, page 7, in particular) that ova from one person is fertilized by another person; hence, the resulting "fertilized ova" which does not include the claimed "autologous stem cells" of the subject being treated by the claimed inventive method is persuasive.

However, applicant fails to recognize that the cell preparations of Marshall et al are likely to contain autologous stem cells at least to some extent inasmuch as the cells such as keratinocytes and fibroblasts are derived from the autologous epidermis (see, e.g., col. 4, lines 55-59; and column 6, lines 47-50, in particular). That epidermal tissue, which is the source for keratinocytes and fibroblasts, contains stem cells is recognized in the art (see evidentiary support and disclosure by Watt, [U2]; summary, and page 831, right column, 2nd paragraph, in particular).

In this regard, it is also noted that applicant has not provided unexpected results for the use of stem cells in the process of dispersing living cells.

The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. *In re Dill*, 202 USPQ 805 (CCPA, 1979), *In re Lindner* 173 USPQ 356 (CCPA 1972), *In re Hyson*, 172 USPQ 399 (CCPA 1972), *In re Boesch*, 205 USPQ 215, (CCPA 1980), *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983), *In re Clemens*, 206 USPQ 289 (CCPA 1980). It should be

clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim.

Therefore the rejection is deemed proper and it is adhered to.

Pertinent Prior Art Not Relied Upon in Rejections

1. **ROLLAND et al (US Patent 7,144,729 B2; filed on Dec. 19, 2002)**, Methods and compositions for tissue regeneration (discloses a method of dispersing isolated, living cell suspensions containing keratinocytes and fibroblast cells, or a mixture thereof onto a wound site using a suitable spray applicator, with or without fibrin glue, with or without scaffold, or dermal allografts, wherein the order of spraying the components can be readily modified or rearranged depending on the need; see abstract, summary of the invention, figures 4-6, column 7, 21-22, 25-26, and examples such as examples 16-17, in particular).
2. **GRANT I. et al.** The co-application of sprayed cultured autologous keratinocytes and autologous fibrin sealant in a porcine wound model, *British J. of Plastic Surgery*, 2002, 55: 219-227 (see summary, materials and methods, in particular).
3. **NAVARRO F.A. et al.** Sprayed keratinocytes suspensions accelerate epidermal coverage in a porcine microwound model, *J. Burn Care Rehabil.*, 2000, 21: 513-518 (see abstract and introduction on page 513, Material and Methods, figure 1, and cited reference 8, in particular).
4. **NAVARRO F.A. et al.** Melanocyte repopulation in full-thickness wounds using a cell spray apparatus, *J. Burn Care Rehabil.*, 2001, 22: 41-46 (see abstract on page 41, and materials & methods, in particular).

Conclusion

NO claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyendra K. Singh whose telephone number is 571-272-8790. The examiner can normally be reached on 9-5MF.


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Satyendra K. Singh
Patent Examiner
Art Unit 1657



IRENE MARX
PRIMARY EXAMINER